

Molecular complexity of voltage-gated sodium channels

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Ion channels are information transmitters of living cells. Ion channel defects appear in a broad range of diseases including epilepsy, migraine, diabetes, hypertension, cardiac arrhythmia, and neuropathic pain. The socioeconomic burden coming from these diseases is significant and affects all aspects of a patient's everyday life, as well as, of their family members. One of the scopes of biomedical research targeting ion channels is to improve diagnostics and develop therapeutic agents and strategies for counteraction, or at least, management of aforementioned diseases. In this Dissertation, we focus on a specific type of ion channels, namely, on voltage-gated sodium channels (VGSCs), which are known to play a key-role in human pain pathophysiology. Results and findings of this Dissertation provide with novel insight into how VGSCs remain functionally-stable within the cell membrane, as well as, into how genetically-caused defects affecting VGSC structure relate to neuropathic pain disease. The main impact of this Dissertation is an improvement in the diagnostic pipeline of inherited neuropathic pain diseases achieved by increasing speed and accuracy of diagnostics while lowering their cost. This is crucial for patients and their family members as it can lead to faster and more accurate genetic counseling and disease diagnosis. Finally, a secondary impact of this Dissertation is that it enriches our knowledge of ion channels as complex systems which, in turn, can prepare the ground for theoretical and computational approaches investigating fine-tuning phenomena in pore-forming molecules to flourish.